

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	36.23	203.38
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.25	-5.25

STN INTERNATIONAL LOGOFF AT 10:22:51 ON 24 APR 2006

10/542,724 YONG CHU 4-24-2006

\$%^STN;HighlightOn=;HighlightOff=;

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID: ssptaylc1626

PASSWORD :

TERMINAL (ENTER 1, 2, 3, OR ?):2

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 DEC 23 New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/USPAT2
NEWS 4 JAN 13 IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 5 JAN 13 New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 6 JAN 17 Pre-1988 INPI data added to MARPAT
NEWS 7 JAN 17 IPC 8 in the WPI family of databases including WPIFV
NEWS 8 JAN 30 Saved answer limit increased
NEWS 9 FEB 21 STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 10 FEB 22 The IPC thesaurus added to additional patent databases on STN
NEWS 11 FEB 22 Updates in EPFULL; IPC 8 enhancements added
NEWS 12 FEB 27 New STN AnaVist pricing effective March 1, 2006
NEWS 13 FEB 28 MEDLINE/LMEDLINE reload improves functionality
NEWS 14 FEB 28 TOXCENTER reloaded with enhancements
NEWS 15 FEB 28 REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 16 MAR 01 INSPEC reloaded and enhanced
NEWS 17 MAR 03 Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 18 MAR 08 X.25 communication option no longer available after June 2006
NEWS 19 MAR 22 EMBASE is now updated on a daily basis
NEWS 20 APR 03 New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 21 APR 03 Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS 22 APR 04 STN AnaVist \$500 visualization usage credit offered
NEWS 23 APR 12 LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 24 APR 12 Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS 25 APR 12 Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT <http://download.cas.org/express/v8.0-Discover/>

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FILE 'HOME' ENTERED AT 10:21:22 ON 24 APR 2006

=> file reg
COST IN U.S. DOLLARS
SINCE FILE ENTRY
SESSION
0.21
0.21
FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 10:21:37 ON 24 APR 2006
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 APR 2006 HIGHEST RN 881539-69-1
DICTIONARY FILE UPDATES: 21 APR 2006 HIGHEST RN 881539-69-1

New CAS Information Use Policies, enter **HELP USAGETERMS** for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

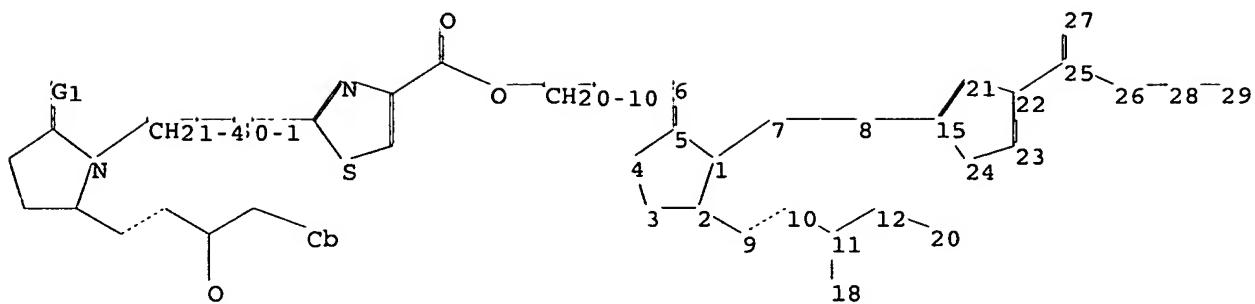
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See **HELP SLIMITS** for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

```
=> Uploading C:\Program Files\Stnexp\Queries\10542724\10542724a.str
```



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chain nodes :
6 7 8 9 10 11 12 18 20 25 26 27 28 29
ring nodes :
1 2 3 4 5 15 21 22 23 24
chain bonds :
1-7 2-9 5-6 7-8 8-15 9-10 10-11 11-12 11-18 12-20 22-25 25-26 25-27
26-28 28-29
ring bonds :
1-2 1-5 2-3 3-4 4-5 15-21 15-24 21-22 22-23 23-24
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 5-6 8-15 9-10 11-18 15-21 15-24 21-22 22-23 23-24
25-26 25-27
exact bonds :
1-7 2-9 7-8 10-11 11-12 12-20 22-25 26-28 28-29

```

G1:O,S

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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 15:CLASS 18:CLASS 20:Atom 21:Atom 22:Atom
23:Atom 24:Atom 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS

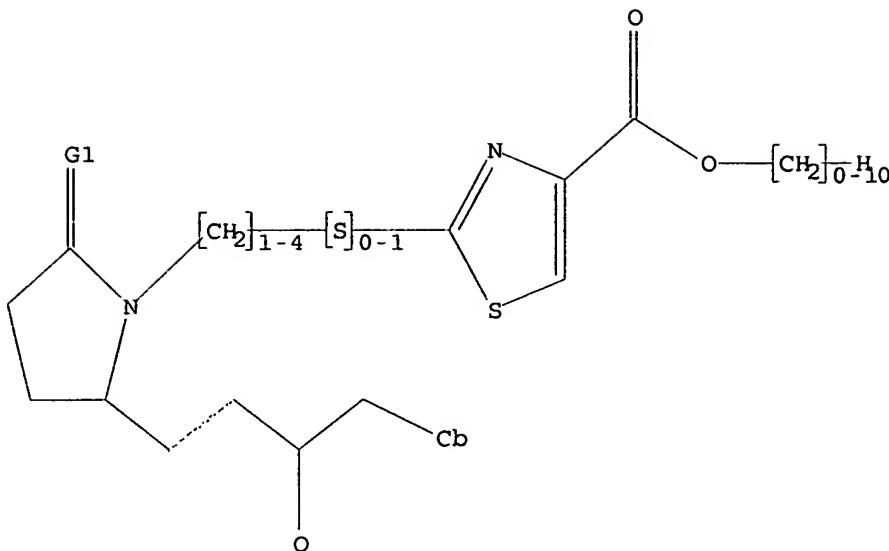
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L1 STRUCTURE UPLOADED

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=> d
L1 HAS NO ANSWERS
L1 STR

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G1 O,S

Structure attributes must be viewed using STN Express query preparation.

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=> s 11
SAMPLE SEARCH INITIATED 10:22:04 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 7 TO ITERATE

100.0% PROCESSED 7 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 7 TO 298
PROJECTED ANSWERS: 3 TO 163
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L2 3 SEA SSS SAM L1

```
=> s 11 full
FULL SEARCH INITIATED 10:22:09 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 91 TO ITERATE

100.0% PROCESSED 91 ITERATIONS 40 ANSWERS
SEARCH TIME: 00.00.01
```

L3 40 SEA SSS FUL L1

```
=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
                           ENTRY SESSION
FULL ESTIMATED COST      166.94 167.15
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FILE 'CAPLUS' ENTERED AT 10:22:19 ON 24 APR 2006
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FILE COVERS 1907 - 24 Apr 2006 VOL 144 ISS 18
FILE LAST UPDATED: 23 Apr 2006 (20060423/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolICY.html>

=> s 13
L4 7 L3

=> d ibib abs hitstr tot

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2006151237 CAPLUS
 DOCUMENT NUMBER: 144:205827
 TITLE: Preventive and/or remedy for hyperkalemia containing EP4 agonist
 INVENTOR(S): Kawauchi, Atsukazu; Suzuki, Yuichi; Maruyama, Takayuki
 PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 111 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006016695	A1	20060216	WO 2005-JP14885	20050809
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GH, GO, GW, ML, MR, NE, SH, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	PRIORITY APPLN. INFO.: JP 2004-232984 A 20040810		

AB Disclosed is a preventive and/or remedy for hyperkalemia and a potassium excretion promoter containing an prostaglandin receptor EP4 agonist. Because of promoting potassium excretion, an EP4 agonist is useful as a preventive and/or remedy for hyperkalemia. A selective EP4 agonist is useful as a preventive and/or remedy for hyperkalemia having no side effect. Furthermore, an EP4 agonist is useful in ameliorating various symptoms of hyperkalemia (for example, sensation abnormality, error of perception, sense of exhaustion, muscle paralysis, nausea, vomiting, abdominal pain, diarrhea, arrhythmia, atrioventricular block, ventricular fibrillation, atrial fibrillation, asystole, respiratory arrest and/or respiratory distress and so on). For example, the EP4 agonistic effect of [13-[(1R,2S,3R)-3-hydroxy-2-[(1E,3S)-3-hydroxy-4-[(3-

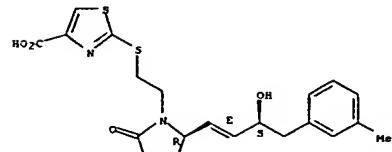
(methoxymethyl)phenyl]but-1-enyl]-5-exocyclopentylsulfanyl]propyl]sulfanylic acid (1) was in vitro examined. Also a tablet containing 1 30 µg/tablet was formulated.

IT 494223-86-8 494223-92-6
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preventive and/or remedy for hyperkalemia containing EP4 agonist)

RN 494223-86-8 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

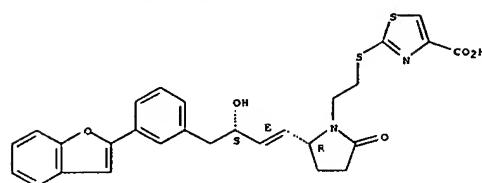
Absolute stereochemistry.
 Double bond geometry as shown.

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 494223-92-6 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-4-[(3-(2-benzofuranyl)phenyl]-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

(methoxymethyl)phenyl]but-1-enyl]-5-exocyclopentylsulfanyl]propyl]sulfanylic acid (1) was in vitro examined. Also a tablet containing 1 30 µg/tablet was formulated.

IT 494223-86-8 494223-92-6
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preventive and/or remedy for hyperkalemia containing EP4 agonist)

RN 494223-86-8 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2006149115 CAPLUS
 DOCUMENT NUMBER: 144:205819

TITLE: Preventive and/or remedy for lower urinary tract diseases containing EP4 agonist
 INVENTOR(S): Okada, Hiroki; Maruyama, Takayuki

PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 119 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006016698	A1	20060216	WO 2005-JP14875	20050809
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GH, GO, GW, ML, MR, NE, SH, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, EM, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	PRIORITY APPLN. INFO.: JP 2004-232985 A 20040810		

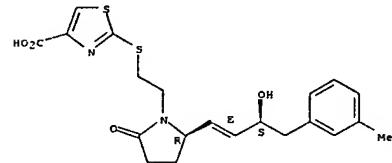
AB Disclosed are (1) a preventive and/or a remedy for lower urinary tract disease such as inflammation in the lower urinary tract, cystitis (interstitial cystitis, etc.) and urethritis; (2) an agent for improving bladder compliance and/or bladder capacity; and (3) an agent for protecting bladder mucosa and/or bladder epithelial cells and/or promoting the regeneration thereof; each containing an EP4 agonist. An EP4 agonist is useful in ameliorating symptoms of lower urinary tract diseases such as (1) frequent urination, (2) urgency of urination, (3) pain in the reproductive organs and/or lower urinary tract (for example, bladder pain, urinary tract pain, vulvar pain, vaginal pain, scrotal pain, perineal pain, pelvic pain, etc.) and/or (4) unpleasantness in the reproductive organs and/or lower urinary tract. Among all, a selective EP4 agonist is useful as a preventive and/or remedy for lower urinary tract diseases having no side effect. For example, the effect of 4-[(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxybut-1-enyl]-5-oxopyrrolidin-1-ylmethanesulfonic acid (1) in cystitis model rats was examined. Also, a tablet containing 1 30 µg/tablet was formulated.

IT 494223-86-8 494223-92-6
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preventive and/or remedy for lower urinary tract diseases containing EP4 agonist)

RN 494223-86-8 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-

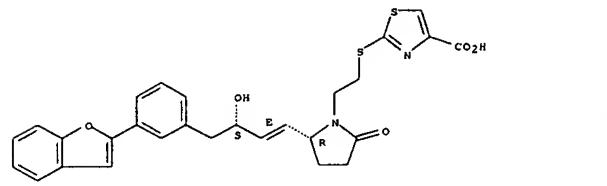
L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
 INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 494223-92-6 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-(2-benzofuranyl)phenyl)-3-hydroxy-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

ACCESSION NUMBER: 2004:633912 CAPLUS

DOCUMENT NUMBER: 141:156958

TITLE: Preparation of 8-azaprostaglandin derivatives as prostaglandin EP4 receptor agonists

INVENTOR(S): Kambe, Tohru; Maruyama, Toru; Kobayashi, Kaoru; Tani, Kousuke; Nakai, Yoshihiko; Nagase, Toshihiko;

Maruyama, Takeyuki; Sakata, Kiyoto; Yoshida, Hideyuki;

PATENT ASSIGNEE(S): Fujisawa, Shinsei; Nishizuka, Aki; Abe, Nobutaka

Ono Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 153 pp.

CODEN: PIKXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004065365	A1	20040805	WO 2004-JP419	20040120
W: AE, BE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CP, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GM, HR, HR, HU, HU, ID, IL, IL, IS, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KE, KE, LC, LC, LS, LS, LT, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MW, MX, ME				
JP 2005104836	A2	20050421	JP 2003-289954	20030808
EP 1586564	A1	20051019	EP 2004-703518	20040120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:		JP 2003-11936	A 20030121	
		JP 2003-269954	A 20030808	
		WO 2004-JP419	W 20040120	

OTHER SOURCE(S): MARPAT 141:156958

GI

postoperative osteogenesis, alternative therapy for bone transplantation.

Thus, (4R,5S,7S)-4-amino-7-hydroxy-8-(3,5-dimethylphenyl)oct-5-enoic acid Et ester hydrochloride (prepn. given) underwent reductive alkylation and cyclization with Me 4-formylmethylbenzoate using sodium triacetoxyborohydride in THF at room temp. overnight to give 2,3,4,5,17,18,19,20-octanor-8-azaprostag-13-enoic acid Me ester deriv. (III; R = OMe) which was saponified by a mixt. of 2 N aq. NaOH soln. and acidified with 2 N aq. HCl soln. to give II (R = OH). II (R = OH) showed the binding activity to prostaglandin EP4 receptor expressed by CHO cells

with Ki of 6.4 nM. A tablet and vial formulation contg. a specific compd. I were described.

IT 494222-47-8 729611-04-5P 729611-06-7P

729611-09-09 729611-12-5P 729611-13-6P

729611-15-8P 729611-16-9P 729611-19-2P

729611-61-4P 729611-62-5P 729611-63-6P

729611-64-7P 729611-65-8P 729611-66-9P

729611-67-0P 729611-68-1P 729611-69-2P

729611-70-5P 729611-71-6P 729611-73-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); B101 (Biological study); PREP (Preparation); USES (Uses)

(preparation of 8-azaprostaglandin derivs. as prostaglandin EP4

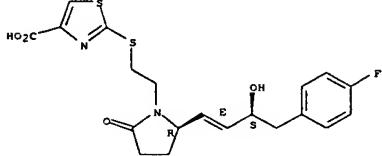
receptor agonists or osteogenesis promoters for preventing and/or treating EP4-mediated diseases or bone diseases)

RN 494222-47-8 CAPLUS

CN 4-Thiazolecarboxylic acid, 2-[(2-((2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl)ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RN 729611-04-5 CAPLUS

CN 4-Thiazolecarboxylic acid, 2-[(2-((2R)-2-[(1E,3S)-3-hydroxy-4-(3-(5-methyl-2-benzoxazolyl)phenyl)-1-butene]-5-oxo-1-pyrrolidinyl)ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

Preparation of 8-azaprostaglandin derivatives as prostaglandin EP4 receptor agonists

Kambe, Tohru; Maruyama, Toru; Kobayashi, Kaoru; Tani, Kousuke; Nakai, Yoshihiko; Nagase, Toshihiko; Maruyama, Takeyuki; Sakata, Kiyoto; Yoshida, Hideyuki;

Fujisawa, Shinsei; Nishizuka, Aki; Abe, Nobutaka

Ono Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 153 pp.

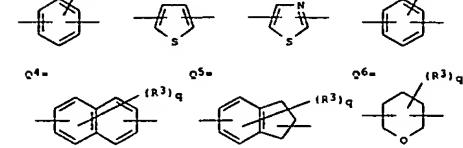
CODEN: PIKXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:



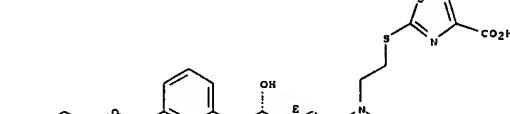
AB Compds. having an 8-azaprostaglandin skeleton represented by the following

general formula (I), salts thereof, solvates thereof, clathrate compds. thereof in cyclodextrin, or prodrugs thereof [wherein a solid line accompanied by a dotted line represents a single or double bond; a wavy line for the OH group represents an α - or β -disposition of a mixture with any α/β ratio thereof; R = Cl-4 alkoxy-carbonyl, tetracyclic; the ring A = O, Cl; O2: R2 = halo, Cl-4 alkyl, Cl-4 alkoxy; P = an integer of 0-6; Y = a bond, S; T = O, S; X = CH2, O, S; ring B = O3, O4, O5, O6; R3 = halo, each mono- to penta-halo-Cl-4 alkyl or -Cl-4 alkoxy; Cl-4 alkoxy-Cl-4 alkyl, Ph, each (un)substituted Ph or 3- to 13-membered bi- or tricyclic heterocycl containing 1-4 heteroatoms selected from N and

S; q = an integer of 0-5] are prepared. These compds. are prostaglandin EP4 receptor agonists and thereby useful in preventing and/or treating EP4-mediated diseases such as immune diseases, asthma, nerve cell death, arthritis, pulmonary injury, pulmonary fibrosis, pulmonary emphysema, bronchitis, chronic obstructive pulmonary disease, liver injury, acute hepatitis, nephritis, renal failure, hypertension, myocardial ischemia, systemic inflammatory reaction syndrome, sepsis, hemophagous syndrome, macrophage activation syndrome, Still's disease, Kawasaki's disease, burn,

systemic granuloma, ulcerative colitis, Crohn's disease, hypercytopenia in dialysis, multiorgan failure, shock and glaucoma. Because of having

an effect of promoting osteogenesis, moreover, they are useful in preventing and/or treating diseases with bone loss (bone diseases such as primary osteoporosis, secondary osteoporosis, bone metastasis of cancer, hypercalcemia, Behcet's disease, bone defect and bone necrosis,

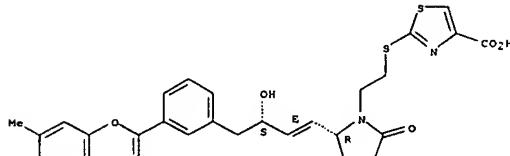


RN 729611-05-7 CAPLUS

CN 4-Thiazolecarboxylic acid, 2-[(2-((2R)-2-[(1E,3S)-3-hydroxy-4-(3-(6-methyl-2-benzoxazolyl)phenyl)-1-butene]-5-oxo-1-pyrrolidinyl)ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

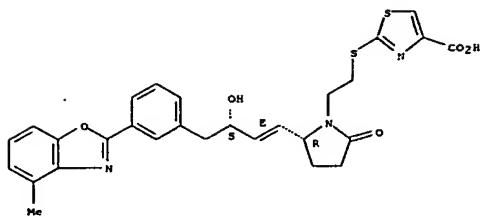


RN 729611-09-0 CAPLUS

CN 4-Thiazolecarboxylic acid, 2-[(2-((2R)-2-[(1E,3S)-3-hydroxy-4-(3-(4-methyl-2-benzoxazolyl)phenyl)-1-butene]-5-oxo-1-pyrrolidinyl)ethyl]thio]- (9CI) (CA INDEX NAME)

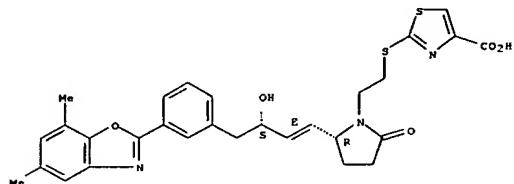
Absolute stereochemistry.

Double bond geometry as shown.



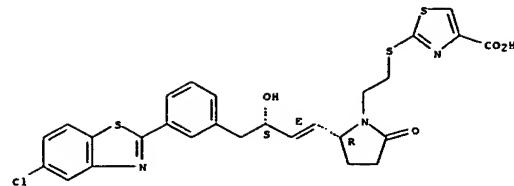
RN 729611-12-5 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-((2R)-2-((1E,3S)-4-[3-(5,7-dimethyl-2-benzoazolyl)phenyl]-3-hydroxy-1-butene)-5-oxo-1-pyrrolidinyl)ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



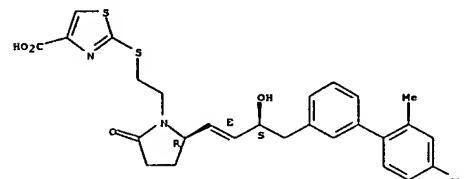
RN 729611-13-6 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-((2R)-2-((1E,3S)-4-[3-(5-chloro-2-benzoazolyl)phenyl]-3-hydroxy-1-butene)-5-oxo-1-pyrrolidinyl)ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



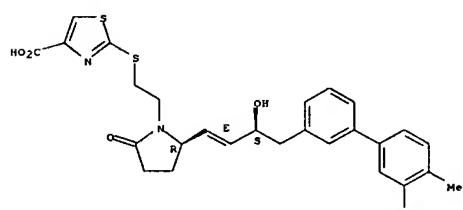
RN 729611-15-6 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-((2R)-2-((1E,3S)-4-(2',4'-dimethyl[1,1'-biphenyl]-3-yl)-3-hydroxy-1-butene)-5-oxo-1-pyrrolidinyl)ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



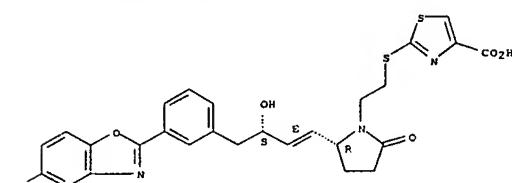
RN 729611-16-9 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-((2R)-2-((1E,3S)-4-(3',4'-dimethyl[1,1'-biphenyl]-3-yl)-3-hydroxy-1-butene)-5-oxo-1-pyrrolidinyl)ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



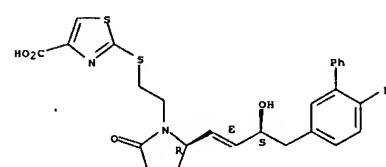
RN 729611-19-2 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-((2R)-2-((1E,3S)-4-[3-(5-chloro-2-benzoazolyl)phenyl]-3-hydroxy-1-butene)-5-oxo-1-pyrrolidinyl)ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



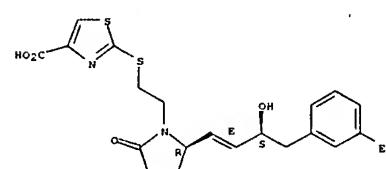
RN 729611-61-4 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-((2R)-2-((1E,3S)-4-(6-fluoro[1,1'-biphenyl]-3-yl)-3-hydroxy-1-butene)-5-oxo-1-pyrrolidinyl)ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



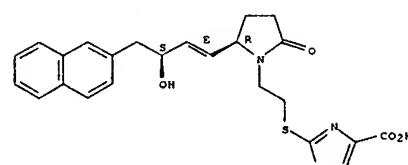
RN 729611-62-5 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-((2R)-2-((1E,3S)-4-(3-ethylphenyl)-3-hydroxy-1-butene)-5-oxo-1-pyrrolidinyl)ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



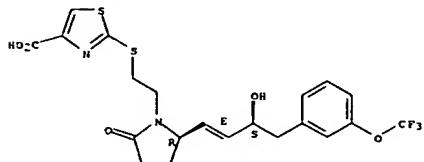
RN 729611-63-6 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-((2R)-2-((1E,3S)-3-hydroxy-4-(2-naphthalenyl)-1-butene)-5-oxo-1-pyrrolidinyl)ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



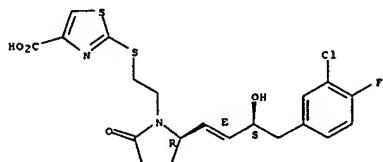
L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-3-hydroxy-4-[(trifluoromethyl)phenyl]-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 729611-65-8 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-4-(3-chloro-4-fluorophenyl)-3-hydroxy-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

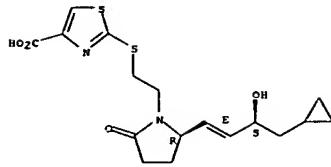


RN 729611-66-9 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-4-cyclopropyl-3-hydroxy-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

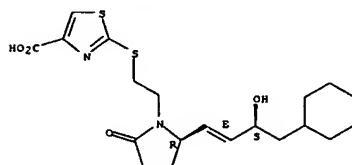
RN 729611-67-0 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-4-cyclohexyl-3-hydroxy-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



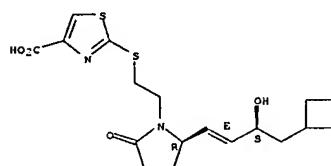
RN 729611-67-0 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-4-cyclohexyl-3-hydroxy-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 729611-68-1 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-4-cyclobutyl-3-hydroxy-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

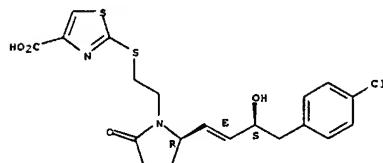
Absolute stereochemistry.
 Double bond geometry as shown.



RN 729611-69-2 CAPLUS

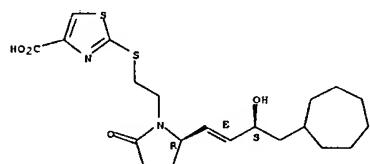
L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-4-(4-chlorophenyl)-3-hydroxy-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 729611-70-5 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-4-cycloheptyl-3-hydroxy-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

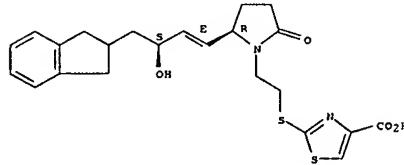
Absolute stereochemistry.
 Double bond geometry as shown.



RN 729611-71-6 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-4-(2,3-dihydro-1H-inden-2-yl)-3-hydroxy-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

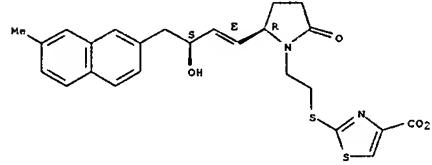
Absolute stereochemistry.
 Double bond geometry as shown.

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 729611-73-8 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(7-methyl-2-naphthalenyl)-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



REFERENCE COUNT: 10 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

14 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:370901 CAPLUS
DOCUMENT NUMBER: 140:391154
TITLE: A preparation of pyrrolidinone derivatives useful as
selective EP4 receptor agonists
INVENTOR(S): Billot, Xavier; Beurard, Jean-Luc; Han, Yongxin;
Young, Robert M.; Colucci, John; Girard, Mario;
Wilson, Marie-Claire
PATENT ASSIGNEE(S): Merck Frost Canada & Co., Can.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIIXDZ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037766	A2	20040506	WO 2003-CAL620	20031023
WO 2004037766	A3	20040930		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, JL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MO, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, US, UZ, VC, VH, YU, ZA, ZM, ZW				
PW: GH, GM, KE, LS, MW, MD, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, CZ, DE, DK, EE, ES, FI, FR, GR, IE, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG				
CA 2502914	AA	20040506	CA 2001-2502914	20031023
AU 2003275840	A1	20040513	AU 2003-275840	20031023
EP 1558602	A2	20050803	EP 2003-809227	20031023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006505572	T2	20060216	JP 2004-545645	20031023
PRIORITY APPLN. INFO.:			US 2002-421402P	P 20021025
			WO 2003-CAL620	W 20031023

OTHER SOURCE(S): MARPAT 140:391154
GI

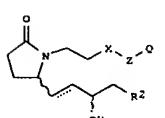
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to pyrrolidinone derivs. of formula I [wherein: Y1
 " (CH₂)₂, CH:CH, 1,2-cyclopropanediyl; Y is C(O) or CH(OH); A is (CH₂)₁₋₄:
 Z = O, S, 1,2-cyclopropanediyl, HC:CH, C.tplbnd.C, or a bond; Q is a
 disubstituted (hetero)aryl ring; W is a bond, unsubstituted Cl-6
 alkylene,
 or Cl-6 alkylene substituted with 1-4 halogen atoms; R1 = OH, CN, CHO,
 etc.; R2 = Cl-6alkyl, (CH₂)₀₋₅-(C6-10aryl), O-C1-10alkyl, etc.; R3 and R4
 are independently selected from halogen, Cl-6alkyl, or R3 and R4,
 together
 with the carbon atom to which they are attached, form a C3-7 cycloalkyl
 ring useful as potent selective agonists of the EP4 subtype of

14 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:757519 CAPLUS
DOCUMENT NUMBER: 139:276612
TITLE: Preparation of hydroxyorgano pyrrolidinones as EPA
receptor selective agonists for the treatment of
hypertension and other disorders
INVENTOR(S): Cameron, Kimberly O'Keefe; Leteker, Bruce Allen;
Knight, Delvin Roscoe, Jr.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003077910	A1	20030925	WO 2003-18844	20030306
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GI, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LF, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MM, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, WF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TZ				
CA 2478653	AA	20030925	CA 2003-2478653	20030306
AU 2003207900	A1	20030929	AU 2003-207900	20030306
EP 1437417	A1	20041222	EP 2003-704902	20030306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IS, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008738	A	20050111	BR 2003-8738	20030306
JP 2005531516	T2	20051020	JP 2003-575963	20030306
US 2003207925	A1	20031106	US 2003-363607	20030312
PRIORITY APPLN. INFO.:			US 2002-365711P	P 20020316

OTHER SOURCE(S): MARPAT 139:276812



AB This invention is directed to hydroxyorgano pyrrolidinones (I; e.g., 4-[3-(2-(3-hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl)propyl]benzoic acid, $\text{X} = \text{O}$, $\text{R} = \text{H}$, as defined below, and in more detail in the claims.

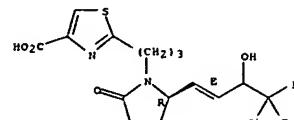
14 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
prostaglandin E2 receptors. The invention compds. are useful in
treatment
of glaucoma and other conditions which are related to the elevated
intraocular pressure in the eye. The invention relates to the use of the
invention compds. for mediating the bone modeling and remodeling
processes

of the osteoblasts and osteoclasts. The invention compds. were tested as EP4 agonists on intraocular pressure in rabbits and monkeys; prostanoid receptor binding assays and bone resorption assays were performed (in a subclass of the invented compds.), agonists have EC50 values from 0.01 μ M to 10 μ M). The synthesized stereoisomeric pyrrolidinones II were prep'd. frm pyrrole deriv. III via oxidn., condensation with PhCF2CO(O)CH2P(O)(OMe)2, keto-group redn. of the obtained unsat'd. ketone IV, alc. protection, N-cleavage, addn. of thiophen deriv. V to the obtained compd. VI, sepn. of the isomers, alc. deprotection, and hydrolysis compd.

IT 685896-09-79
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of pyrrolidinone derivs. useful as selective EP4 receptor agonists)
 RN 685896-09-7 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[3-[(2R)-2-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenvinyl]-5-oxo-1-pyrrolidinyl]vinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
 that are EP4 receptor selective prostaglandin agonists. This invention
 is also directed to pharmaceutical compns. contg. those compds. This invention is also directed to methods of treating hypertension, liver failure, loss of patency of the ductus arteriosus, glaucoma or ocular hypertension. IC50 values for binding of 5-[3-[2S-3R-hydroxy-4-(3-trifluoromethylphenyl)butyl]-5-oxopyrrolidin-1-yl]propyl|thiophene-2-carboxylic acid (II) to various receptors are human EP1 receptor, >1000 nm; rat EP2 receptor, 463 nm; human EP3 receptor, >1000 nm; and rat EP4 receptor, 11 nm. II exhibited an EC50 value of 0.6 nm in an assay involving cAMP elevation in 293S cell lines stably overexpressing recombinant rat EP4 receptors. Results are also presented for the hypotensive effect of the Na salt of II in *in vivo* rabbit and primate models. In I, a prodrug thereof, a pharmaceutically acceptable salt of said compd. or said prodrug or a stereoisomer or diastereomeric mixt. of said compd., prodrug or salt; the dotted line is a bond or no bond; X is -CH2- or O; Z is -(CH2)3, thiienyl, thiazolyl or Ph, provided that when X is O, then Z is phenyl; Q is carboxy, (Cl-C4)alkoxycarbonyl or tetrazolyl;
 R2 is -Ar or -Ar1-V-Ar2; V is a bond, -O-, -OCH2- or -CH2O-. Ar is a partially satd., fully satd. or fully unsatd. 5-8 membered ring
 optionally having 1-4 heteroatoms selected independently from O, S and N, or a bicyclic ring consisting of two fused independently partially satd., fully satd. or fully unsatd. 5-6 membered rings, taken independently,
 optionally having 1-4 heteroatoms selected independently from N, S and O, said partially or fully satd. ring or bicyclic ring optionally having 1-2 exo groups substituted on C or 1-2 exo groups substituted on S. Ar1 and Ar2 are each independently a partially satd., fully satd. or fully unsatd.
 5-8 membered ring optionally having 1-4 heteroatoms selected independently

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
 carbamoyl, mono-N- or di-N,N-(C1-C4)alkylcarbamoyl, cyano, thiol, (C1-C6)alkylthio, (C1-C6)alkylsulfanyl, (C1-C4)alkylsulfenyl and mono-N- or di-N,N-(C1-C4)alkylaminosulfenyl, wherein said alkyl and alkoxy substituents in the definition of Ar1 and Ar2 are optionally substituted on C with up to three fluoro. (a) when X is (CH2)2- and Z is -(CH2)3-, then R2 is not thiienyl, Ph or Ph monosubstituted with chloro, fluoro, Ph, methoxy, trifluoromethyl or (C1-C4) alkyl; and (b) when X is (CH2)2- and Z is -(CH2)3-, and Q is carboxy or (C1-C4) alkoxy carbonyl, then R2 is not (i) (C5-C7)cycloalkyl or (ii) phenyl, thiienyl or furyl each of which may be optionally monosubstituted or disubstituted by one or two substituents selected, independently in the latter case, from halogen atoms, alkyl groups having 1-3 C atoms which may be substituted by one or more halogen atoms, and alkoxy groups having 1-4 C atoms. Although the methods of prepn. are not claimed, 41 example prepn.s. are included.

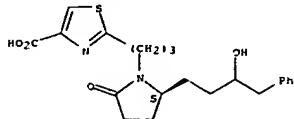
IT 431990-21-59

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses); (intermediate; preparation of hydroxyorgano pyrrolidinones as EP4 receptor selective agonists for treatment of hypertension and other disorders)

RN 431990-21-5 CAPLUS

CN 4-Thiazolecarboxylic acid, 2-[3-[(2S)-2-(3-hydroxy-4-phenylbutyl)-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 431990-26-09

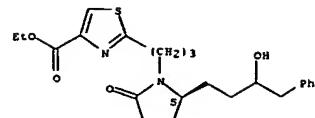
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent); (intermediate; preparation of hydroxyorgano pyrrolidinones as EP4 receptor selective agonists for treatment of hypertension and other disorders)

RN 431990-26-0 CAPLUS

CN 4-Thiazolecarboxylic acid, 2-[3-[(2S)-2-(3-hydroxy-4-phenylbutyl)-5-oxo-1-pyrrolidinyl]propyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



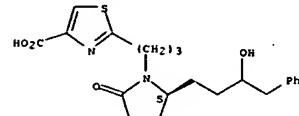
IT 431990-27-19

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses); (preparation of hydroxyorgano pyrrolidinones as EP4 receptor selective agonists for treatment of hypertension and other disorders)

RN 431990-27-1 CAPLUS

CN 4-Thiazolecarboxylic acid, 2-[3-[(2S)-2-(3-hydroxy-4-phenylbutyl)-5-oxo-1-pyrrolidinyl]propyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● Na

REFERENCE COUNT:

5

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003-97322 CAPLUS
 DOCUMENT NUMBER: 138-142493
 TITLE: Remedies for diseases with bone mass loss having EP4 agonist as the active ingredient
 INVENTOR(S): Maruyama, Toru; Kobayashi, Kaoru; Kambe, Tohru; Maruyama, Takayuki; Yoshida, Hideyuki; Nishiura, Akio;
 PATENT ASSIGNEE(S): Abe, Nobutaka
 SOURCE: One Pharmaceutical Co., Ltd., Japan
 DOCUMENT TYPE: PCT Int. Appl., 474 pp.
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 200309072	A1	20030206	WO 2002-JP7385	20020722
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LV, MA, MD, MG, MH, MO, MW, MZ, NO, NQ, OM, PH, PL, PT, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZN, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1417975	A1	20040512	EP 2002-747707	20020722
R: AE, BE, CH, DE, DK, ES, FR, GB, GR, IT, I, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, DK				
BR 2002011364	A	20040713	BR 2002-11364	20020722
ZA 2004000493	A	20050119	ZA 2004-493	20040122
US 2005020686	A1	20050127	US 2004-484500	20040122
NO 2004000331	A	20040323	NO 2004-331	20040123
PRIORITY APPLN. INFO.:			JP 2001-222148	A 20010723
			JP 2001-239895	A 20010807
			JP 2002-56449	A 20020301
			WO 2002-JP7385	W 20020722

OTHER SOURCE(S): MARPAT 138-142493

AB Disclosed are drugs for topical administration which contain an EP4 agonist as the active ingredient for preventing and/or treating diseases in association with bone mass loss. The EP4 agonists typified by compds. with the prostaglandin skeleton have an effect of promoting osteogenesis. Thus, topical administration thereof is highly useful in preventing and/or treating diseases in association with bone mass loss, e.g., bone diseases such as primary osteoporosis, secondary osteoporosis, bone metastasis of cancer, hypercalcemia, Behcet's disease, bone loss and bone necrosis, postoperative osteogenesis, alternative therapy for bone transplantation. A compound (IIIa, Ibu, 13E)-9-oxo-11,15-dihydroxy-16-(3-

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
 methoxymethylphenyl)-17,18,19,20-tetraen-5-thiaprostan-13-enoic acid 2-nonanoyloxyethyl ester was prep'd., and mixed with lactic acid-glycolic acid copolymer to obtain a microsphere. The obtained microsphere was administered to fracture bone part of a rat to examine the bone formation promoting effect.

IT 494222-47-89 494223-71-1P 494223-74-4P

494223-85-79 494223-86-8P 494223-90-4P

494223-91-51 494223-92-6P 494224-07-6P

494224-08-79 494224-09-8P 494224-13-4P

494224-14-59 494224-15-6P 494224-18-9P

494224-19-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses); (remedies for diseases with bone mass loss containing prostaglandin

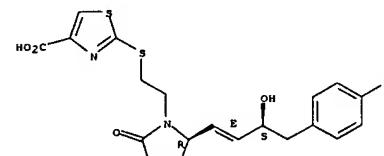
EP4 receptor agonists as active ingredients)

RN 494222-47-8 CAPLUS

CN 4-Thiazolecarboxylic acid, 2-[2-((2R)-2-((3S,4S)-4-(4-fluorophenyl)-3-hydroxy-1-butenoxy)-5-oxo-1-pyrrolidinyl)ethyl]thio- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

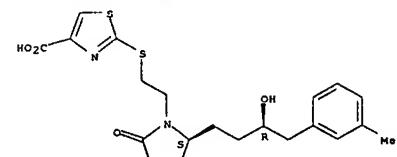
Double bond geometry as shown.



RN 494223-71-1 CAPLUS

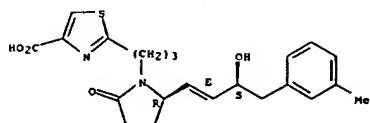
CN 4-Thiazolecarboxylic acid, 2-[2-((2S)-2-((3R)-3-hydroxy-1-(3-methylphenyl)butyl)-5-oxo-1-pyrrolidinyl)ethyl]thio- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



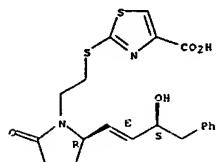
L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
 RN 494223-74-4 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 494223-85-7 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

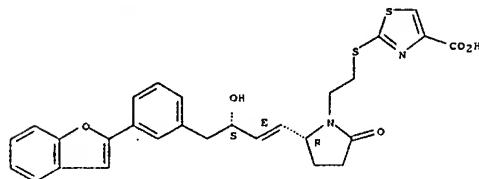


RN 494223-86-0 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butenyl]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

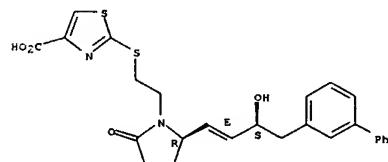
L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
 RN 494223-92-6 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-4-(3-(2-benzofuranyl)phenyl)-3-hydroxy-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 494224-07-6 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-4-(1,1'-biphenyl)-3-yl]-3-hydroxy-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

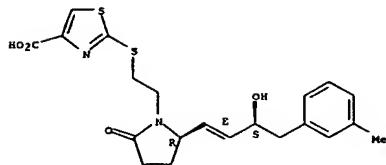
Absolute stereochemistry.
 Double bond geometry as shown.



RN 494224-08-7 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(4'-methyl-1,1'-biphenyl)-3-yl]-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

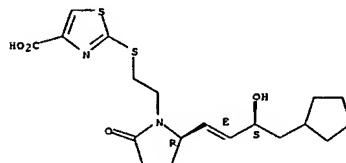
Absolute stereochemistry.
 Double bond geometry as shown.

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



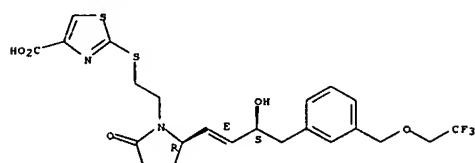
RN 494223-90-4 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-4-cyclopentyl-3-hydroxy-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

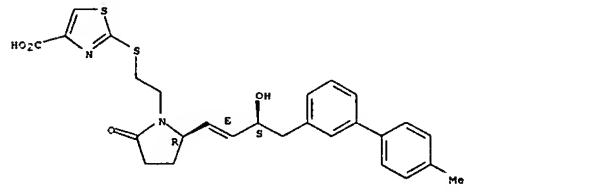


RN 494223-91-5 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-(2,2,2-trifluoroethoxy)methylphenyl)-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

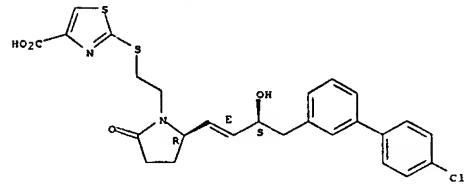


L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



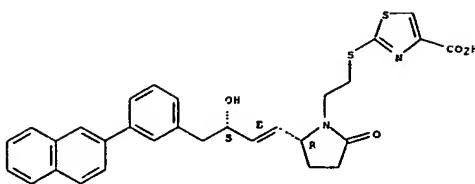
RN 494224-09-8 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-4-(4'-chloro-1,1'-biphenyl)-3-yl]-3-hydroxy-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



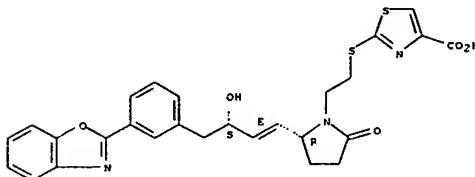
RN 494224-13-4 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[(2-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-naphthalenyl)-1-butene]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



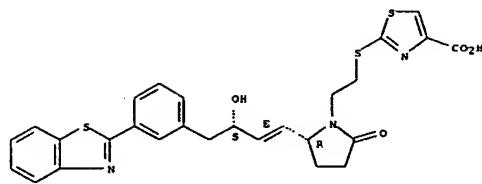
RN 494224-14-5 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[[2-[(2R)-2-[(1E,3S)-4-[(3-(2-benzoazolyl)phenyl)-3-hydroxy-1-but enyl]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



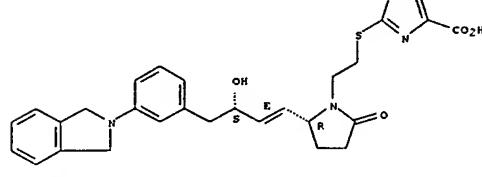
RN 494224-15-6 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[[2-[(2R)-2-[(1E,3S)-4-[(3-(2-benzoazolyl)phenyl)-3-hydroxy-1-but enyl]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



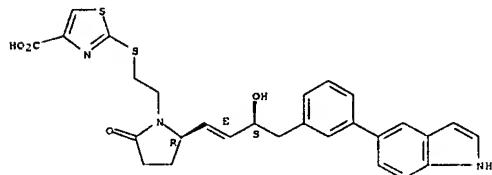
RN 494224-18-9 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[[2-[(2R)-2-[(1E,3S)-4-[(3-(1,3-dihydro-2H-isoindol-2-yl)phenyl)-3-hydroxy-1-but enyl]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 494224-19-0 CAPLUS
 CN 4-Thiazolecarboxylic acid, 2-[[2-[(2R)-2-[(1E,3S)-3-hydroxy-4-[(3-(1H-indol-5-yl)phenyl)-1-but enyl]-5-oxo-1-pyrrolidinyl]ethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 2002408643 CAPLUS

DOCUMENT NUMBER: 137:6083

TITLE: Preparation of EP4 receptor selective agonists for the

INVENTOR(S): Cameron, Kimberly O'Keefe; Leitke, Bruce Allen
 Pfizer Products Inc., USA

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 122 pp.

CODEN: PIXX02

DOCUMENT TYPE: Patent

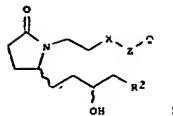
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002042268	A2	20020530	WO 2001-1B2073	20011105
WO 2002042268	A3	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, CA 2429850	AA	20020530	CA 2001-2429850	20011105
AU 2002010846	A5	20020603	AU 2002-10848	20011105
EP 1339678	A2	20030903	EP 2001-978757	20011105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BB 2001015687	A	20030909	BR 2001-15687	20011105
EE 200300246	A	20031015	EE 2003-246	20011105
JP 2004521869	T2	20040722	JP 2002-544404	20011105
NZ 525164	A	20050429	NZ 2001-525164	20011105
US 2002065308	A1	20020530	US 2001-990556	20011121
US 6552067	B2	20030422		
US 2003149086	A1	20030807	US 2002-326366	20021220
US 6747054	B2	20040608		
BG 107697	A	20040130	BG 2003-107697	20030403
ZA 2003002803	A	20040413	ZA 2003-2803	20030410
NO 2003002360	A	20030723	NO 2003-2360	20030526
US 2004259921	A1	20041223	US 2003-668633	20030923
PRIORITY APPN. INFO.:			US 2000-253275P	P 20001127
			WO 2001-1B2073	W 20011105
			US 2001-990556	A3 20011121
			US 2002-326366	A3 20021220

OTHER SOURCE(S): MARPAT 137:6083
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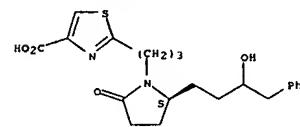


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AB This invention is directed to EP4 receptor selective prostaglandin agonists I (e.g. 4-[3-[2-(3-hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl]propyl]benzoic acid), wherein R2, X, Z and C are defined below and in more detail in the claims. This invention is also directed to pharmaceutical compns. containing those compds. This invention is also directed to methods of treating conditions which present with low bone mass, particularly osteoporosis, frailty, an osteoporotic fracture, a bone defect, childhood idiopathic bone loss, alveolar bone loss, mandibular bone loss, bone fracture, osteotomy, bone loss associated with periodontitis, or prosthetic ingrowth in a mammal comprising administering those compds. Although biol. testing protocols are included, no test results are given. In I, a prodrug thereof, a pharmaceutically acceptable salt of said compound, or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt; the dotted line is a bond or no bond; X is -CH2- or O; Z is -(CH2)3-, thiienyl, thiazolyl or Ph, provided that when X is O, then Z is phenyl; Q is carboxy, (C1-C4)alkoxycarbonyl or tetrazolyl; R2 is -Ar or -Ar1-V-Ar2; V is a bond, -O-, -OCH2- or -CH2O-. Ar is a partially saturated, fully saturated or fully unsatd. 5-8 membered ring optionally having 1-4 heteratoms selected independently from O, S and N, or a bicyclic ring consisting of two fused independently partially saturated, fully saturated or unsatd. 5-6 membered rings, taken independently, optionally having 1-4 heteratoms selected independently from O, S and N, said partially or fully saturated ring or bicyclic ring optionally having 1-2 oxo groups substituted on C or 1-2 oxo groups substituted on S. Ar1 and Ar2 are each independently a partially saturated, fully saturated or fully unsatd. 5-8 membered ring optionally having 1-4 heteratoms selected independently from O, S and N, said partially or fully saturated ring optionally having 1-2 oxo groups substituted on C or 1-2 oxo groups substituted on S. Ar is optionally substituted on C or H, on one ring if the moiety is monocyclic, or on one or both rings if the moiety is bicyclic, with up to three substituents per ring each independently selected from hydroxy, halo, carboxy, (C1-C7)alkoxy, (C1-C4)alkoxycarbonyl, (C1-C7)alkyl, (C2-C7)alkenyl, (C3-C7)cycloalkyl, (C1-C4)cycloalkenyl, (C1-C7)cycloalkyl(C1-C4)alkenyl, formyl, (C1-C8)alkanoyl, (C1-C6)alkanoyl(C1-C6)alkyl, (C1-C4)alkanoylaminino, (C1-C4)alkoxycarbonylaminino, hydroxysulfonyl, aminocarbonylaminino or mono-N-, di-N,N'- or tri-N,N,N'-(C1-C4)alkyl substituted aminocarbonylaminino, sulfonamido, (C1-C4)alkylsulfonamido, amino, mono-N- or di-N,N-(C1-C4)alkylaminino, carbamoyl, mono-N- or di-N,N-(C1-C4)alkylthio, (C1-C6)alkylsulfinyl, (C1-C4)alkylsulfonyl and mono-N- or di-N,N-(C1-C4)alkylaminosulfonyl, wherein said alkyl and alkoxy substituents in the definition of Ar are optionally substituted on C with up to three fluoro. Ar1 and Ar2 are independently optionally substituted on C or N with up to three substituents each independently selected from hydroxy, halo, carboxy, (C1-C7)alkoxy, (C1-C4)alkoxy(C1-C4)alkyl, (C1-C7)alkyl, (C2-C7)alkenyl, (C3-C7)cycloalkyl, (C3-C7)cycloalkyl(C1-C4)alkyl, (C3-C7)cycloalkyl(C1-C4)alkanoyl, formyl, (C1-C8)alkanoyl, (C1-C6)alkanoyl(C1-C6)alkyl, (C1-C4)alkanoylaminino, (C1-C4)alkoxycarbonylaminino, hydroxysulfonyl, aminocarbonylaminino or mono-N-, di-N,N'- or tri-N,N,N'-(C1-C4)alkyl substituted aminocarbonylaminino, sulfonamido, (C1-C4)alkylsulfonamido, amino, mono-N- or di-N,N-(C1-C4)alkylaminino, carbamoyl, mono-N- or di-N,N-(C1-C4)alkylthio, (C1-C6)alkylsulfinyl, (C1-C4)alkylsulfonyl and mono-N- or di-N,N-(C1-C4)alkylaminosulfonyl, wherein said alkyl and alkoxy substituents in the definition of Ar1 and Ar2 are optionally substituted on C with up to three fluoro. (a) when X is -(CH2)3- and Z is -(CH2)3-, then R2 is not thiienyl, Ph or Ph monosubstituted with chloro, fluoro, Ph, methoxy, trifluoromethyl or (C1-C4)alkyl; and (b) when X is (CH2)3-, Z is -(CH2)3-, and Q is carboxy or (C1-C4)alkoxycarbonyl, then R2 is not (i) (C5-C7)cycloalkyl or (i) phenyl, thiienyl or furyl each of which may be optionally monosubstituted or disubstituted by one or two substituents selected, independently in the latter case, from halogen atoms, alkyl groups having 1-3 C atoms which may be substituted by one or more halogen atoms, and alkoxy groups having 1-4 C atoms. Although the methods of prepns. are not claimed, 41 example preps. are included.

IT 431990-21-5P, 2-[3-((2S)-3-Hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl]propylthiazole-4-carboxylic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses); intermediate; preparation of EP4 receptor selective agonists for treatment of osteoporosis
RN 431990-21-5 CAPLUS
CN 4-Thiazolecarboxylic acid, 2-[(2S)-2-(3-hydroxy-4-phenylbutyl)-5-oxo-1-pyrrolidinyl]propyl-, (9CI) (CA INDEX NAME)

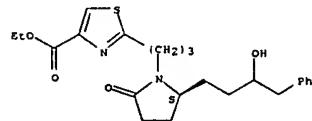
Absolute stereochemistry.



IT 431990-26-0P, 2-[3-((2S)-3-Hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl]propylthiazole-4-carboxylic acid ethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent); intermediate; preparation of EP4 receptor selective agonists for treatment

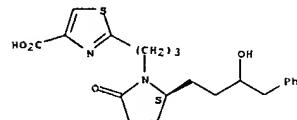
of osteoporosis;
RN 431990-26-0 CAPLUS
CN 4-Thiazolecarboxylic acid, 2-[(2S)-2-(3-hydroxy-4-phenylbutyl)-5-oxo-1-pyrrolidinyl]propyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 431990-27-1P, Sodium salt of 2-[3-((2S)-3-hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl]thiazole-4-carboxylic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses); intermediate; preparation of EP4 receptor selective agonists for treatment of osteoporosis
RN 431990-27-1 CAPLUS
CN 4-Thiazolecarboxylic acid, 2-[(2S)-2-(3-hydroxy-4-phenylbutyl)-5-oxo-1-pyrrolidinyl]propyl-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● Na